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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,570	08/25/2006	David H. Wagner	059742-5001	1193

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
03/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,570	WAGNER, DAVID H.	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Amendment Entry

1. Applicant's response and amendment filed 11/28/08 is acknowledged (Paper filed 11/28/07). In the amendment filed therein the specification and claim 3 were modified.

2. Claims 9-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/23/07. Currently claims 1-8 and 27 are under consideration.

3. Rejections and/or objections of record not reiterated herein have been withdrawn.

REJECTIONS WITHDRAWN

4. Applicant contends that the reference to Berner et al. does not anticipate the instant invention because CD4+Cd40+ is not the same molecule as CD40L. This argument was carefully considered and found persuasive. Accordingly the rejection of claims 1, 4, 7 and 8 under 35 USC 102(b) over Berner et al. is hereby withdrawn.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787).

Wagner et al. disclose antibody staining and flow cytometry procedures to detect $CD4^{+}CD40^{+}$ T cells. See page 3782 – 2nd column. T cells were isolated from spleen, thymus, or pancreas of diabetic NOD (nonobese diabetic) mice. The NOD mouse has been used extensively as a model for human type 1 autoimmune diabetes. See page 3782 1st column 3rd paragraph. The cells were triple stained with phycoerytherin vs. directly conjugated anti-CD4 and FITC-conjugated anti-CD40. The researcher found that CD40 is functionally expressed on CD4+ T cells and may have an important role in the pathogenesis of autoimmune diseases. See page 3783 1st column – Results. The data suggested that $CD40^{lo}CD4^{hi}$ T cells were 32% in the periphery of spleen. Whereas only 7% of the T cells from BALB/control mice were $CD4^{lo}CD40^{hi}$. See page 3786 1st column and page 3787. The diabetogenic T cell clones expressed CD40 while the nondiabetogenic T cell clones (controls) were $Cd40^{-}$. See page 3783 – Results and figure 1.

Response to Arguments

Applicant contends that Wagner et al. neither disclose nor suggest that an increased level of $CD4^{lo}CD40^{hi}$ T cells in the blood sample of a subject is indicative of an auto-immune disease like diabetes. This argument was carefully considered but not found persuasive because $CD4^{lo}CD40^{hi}$ encompasses the same cell population as $CD4^{+}CD40^{+}$ cells. See the instant

specification page 9 lines 30-31, for example.

Wagner et al. disclose that auto-immune mice have a *large* population of $CD4^+$ cells that express CD40. The autoimmune prone strains of mice had substantially large numbers of $CD40^+CD4^+$ T cells in their periphery. See page 3782, 1st column 2nd paragraph. In addition, diabetogenic T cell clones of either Th1 or Th2 phenotype are CD40-positive, whereas nondiabetogenic clones (control) are CD40-negative. See abstract.

Applicant also contends that Wagner et al. do not teach or suggest increased levels of $CD4^{lo}CD40^{hi}$ T cells as markers for autoimmune diseases, but rather that $CD4^{lo}CD40^{hi}$ cells are increased as a percentage of T cells in NOD mice. This argument was carefully considered but not found persuasive because Wagner et al. disclose that purified T cells form the spleens of diabetic NOD mice were compared to age-matched BALB/C controls. In the diabetic NOD animals, 32% of the purified T cells were $CD4^{lo}CD40^{hi}$, while only 7% of the T cells from the BALB/C mice controls were $CD4^{lo}CD40^{hi}$. Because 32% is an increased over 7%, the reference reads on the instant claims directed to an "increased level of $CD4^{lo}CD40^{hi}$ T cells.

In considering the anticipatory effect of a reference, not only its specific teaching but also the inferences which one skilled in the art would reasonably be expected to draw therefrom should be taken into account. *In re Preda* (CCPA 1968) 401 F2d 825, 159 USPQ 342.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102((e), f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 2, 3 and 6 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787) in view of Jeffery PK (Novartis Foundation Symposium, 2001, Vol.234, page 149-161, Abstract Only) and Wald et al. (FASEB, 2003, 17(7), page C177, Abstract).

Please see Wagner et al. as set forth above.

Wagner et al. differ from the instant invention in not specifically teaching the measurement of emphysema and at least one cytokine.

However, Jeffery PK teaches that cytotoxic T lymphocytes CD8 are involved in emphysema and asthma is a helper T cell CD4 type inflammatory disorder. However, there may be important similarities and overlap, particularly in more severe asthma. Gene expression for IL-4 and IL-5 were seen in the disorders and it is speculated that the CD4/CD8 T lymphocyte ratio is relevant and important to the development of COPDs. See abstract.

Although Jeffery PK is silent with respect to $CD4^+CD40^+$ cells, Wald et al. teaches that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further, these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the immunoassay measurements of $CD4^+CD40^+$ cells as taught by Wagner et al. to measure emphysema and cytokine expression as taught by Jeffery and Wald et al. because Jeffrey PK taught that CD4 is involved in the development of COPDS (emphysema/asthma) and the disorders may have similarities and overlap, while Wald et al. taught that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

One of ordinary skill in the art would have been motivated to do this in order to evaluate COPDs for evaluation and treatment.

Response to Arguments

Applicant argues that the deficiencies of Wagner et al. are not cured by the addition of Jeffrey and Waid et al. This argument was carefully considered but not found persuasive because the reference of Wagner et al. has been maintained *a priori*. Please see discussion above. Accordingly the rejection is maintained.

It is noted that the examiner's rejection included a typo reciting "35 USC 103(b)" in stead of "35 USC 103(a)". However, the appropriate heading was cited and the rejection of record has remained the same. There is no "new ground" of rejection when the "basic thrust" of the rejection is the same. *Ex parte Maas*, 9 USPQ.2d 1746 (Bd. Pat. App. & Int. 19870.

III. Claim 27 is rejected under 35 U.S.C.103 (a) as being unpatentable over Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787) in view of Foster et al. (U.S. Patent #4,444,879).

Please see Wagner et al. as set forth above.

Although Wagner et al. teach the reagents required by the claims; they do not specifically teach the reagents in kit configurations. In other words, the reference fails to teach the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Wagner et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

Response to Arguments

Applicant argues that the deficiencies of Wagner et al. are not cured by the addition of Foster et al. This argument was carefully considered but not found persuasive because the

reference of Wagner et al. has been maintained *a priori*. Please see discussion above. Accordingly the rejection is maintained.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).

See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

IV. Claims 1, 4, 5, 7, 8, and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/399,384. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the measurement of the same cells. The instant invention recites the measurement of $CD4^{lo}CD40^{hi}$ T cells, while application number 11/399,384 recited $CD^{+}CD40^{+}$T cells. Both disclosures teach that these cells are the same. See page 18 section 0058 in application number 11/399,384 and page 9 lines 30-33 in application number 10/563,570. The terms are taught to be interchangeable.

Accordingly, the methods are not patentably distinct from each other. The claims of application number 11/399,384, encompasses the instantly claimed invention. Accordingly, the methods are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

V. Claims 2, 3, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/399,384 in view of Jeffery PK (Novartis Foundation Symposium, 2001, Vol.234, page 149-161, Abstract Only) and Wald et al. (FASEB, 2003, 17(7), page C177, Abstract).

Please see Application No. 11/399,384 as set forth above.

Application No. 11/399,384 differs from the instant invention in not specifically teaching the measurement of emphysema and at least one cytokine.

However, Jeffery PK teaches that cytotoxic T lymphocytes CD8 are involved in emphysema and asthma is a helper T cell CD4 type inflammatory disorder. However, there may be important similarities and overlap, particularly in more severe asthma. Gene expression for IL-4 and IL-5 were seen in the disorders and it is speculated that the CD4/CD8 T lymphocyte ratio is relevant and important to the development of COPDs. See abstract.

Although Jeffery PK is silent with respect to $CD4^{+}CD40^{+}$ cells, Wald et al. teaches that $CD4^{+}CD40^{+}$ T cells are involved in the progression of asthma. Further, these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the immunoassay measurements of $CD4^{+}CD40^{+}$ cells as taught Application No. 11/399,384 to measure emphysema and cytokine expression as taught by Jeffery and Wald et al. because Jeffrey PK taught that CD4 is involved in the development of COPDS (emphysema/asthma) and the disorders may have similarities and overlap, while Wald et al. taught that $CD4^{+}CD40^{+}$ T cells are involved in the progression of asthma. Further these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

One of ordinary skill in the art would have been motivated to do this in order to evaluate COPDs for evaluation and treatment. This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicant contends that the present application is not an obvious variation of the claimed invention in US Application No. 11/399,384 because the application recites the species-diabetes. While the instant claims read on the genus autoimmune diseases. This argument was carefully considered and not found persuasive because the claims are not patentably distinct. The claims to the genus encompass the species as set forth above.

Applicant also argues that instant application has an earlier filing date. This was not found persuasive because the ODP is a provisional rejection. Accordingly the rejections are maintained.

8. For reasons aforementioned and already of record, no claims are allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

10. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Mehling et al. (Critical Reviews in Biochemistry and Molecular Biology, 38(1), pages 1-21, 2/1/03) disclose dendritic cells as regulators of autoimmune responses.

B. Valentini et al. (Journal of Autoimmunity, 2000, Vol.15, pages 61-66) teach the increased expression of CD40 ligand in activated CD4+ cells in sclerosis patients.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lisa V. Cook/
Primary Examiner, Art Unit 1641

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641